What is claimed is:

1. A variant thrombin comprising an amino acid sequence having the substitutions W215A and E217A, wherein the amino acid sequence is at least 80% identical to the sequence set forth in SEQ ID NO: 3.

2. The variant thrombin according to Claim 1 comprising a thrombin B-chain comprising the amino acid sequence as set forth in SEQ ID NO: 4.

3. The variant thrombin according to Claim 1, wherein the variant thrombin is encoded by a nucleic acid comprising the sequence as set forth in SEQ ID NO: 5, or a degenerate variant thereof.

4. The variant thrombin according to Claim 2, wherein the variant thrombin is encoded by a nucleic acid comprising the sequence as set forth in SEQ ID NO: 6, or a degenerate variant thereof.

5. The variant thrombin according to Claim 1 having a PA/FC ration greater than 1.0.

6. The variant thrombin according to Claim 1 having a PA/FC ration greater than 150.

7. The variant thrombin according to Claim 1, wherein the variant thrombin is expressed from a recombinant nucleic acid within a cell.

8. The variant thrombin according to Claim 7, wherein the recombinant nucleic acid comprises a sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6, or a degenerate variant thereof.

9. A nucleic acid encoding a variant thrombin and comprising a nucleic acid selected from SEQ ID NO: 5 and SEQ ID NO: 6, or a degenerate variant thereof.

10. The nucleic acid according to Claim 9, wherein the nucleic acid is in an expression cassette.

11. The nucleic acid according to Claim 10, wherein the expression cassette is in a vector.

12. A cell having a nucleic acid comprising the sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6, or a degenerate variant thereof, and capable of producing a variant thrombin protein according to Claim 9.

13. A physiologically acceptable composition comprising:

(a) a variant thrombin, wherein the variant prothrombin has the amino acid substitution W215A and is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 1; and

(b) at least one pharmaceutically acceptable carrier.

14. The physiologically acceptable composition according to Claim 13, wherein the variant thrombin comprises the amino acid sequence set forth in SEQ ID NO: 1.

15. The physiologically acceptable composition according to Claim 13, wherein the variant thrombin comprises the amino acid sequence set forth in SEQ ID NO: 2.

16. A physiologically acceptable composition comprising:

(a) a variant thrombin, wherein the variant prothrombin has the amino acid substitutions W215A and E217A, and is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 3; and

(b) at least one pharmaceutically acceptable carrier.

17. The physiologically acceptable composition according to Claim 16, wherein the variant thrombin has the amino acid substitutions W215A and E217A, and comprises the amino acid sequence set forth in SEQ ID NO: 3.

18. The physiologically acceptable composition according to Claim 16, wherein the variant thrombin has the amino acid substitutions W215A and E217A, and comprises the amino acid sequence set forth in SEQ ID NO: 4.

19. A method of inhibiting the formation of a thrombus, comprising the steps of:

(a) delivering to the blood of an animal or human a physiologically acceptable composition comprising an effective amount of a variant thrombin with substantially reduced procoagulant activity, wherein the variant thrombin has the amino acid substitution W215A and comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 1; and

(b) allowing the variant thrombin to activate protein C, thereby inhibiting thrombus formation.

20. The method according to Claim 19, further comprising the step of administering to the animal or human a variant prothrombin capable of cleavage to the variant thrombin.

21. The method according to Claim 19, wherein the variant thrombin comprises the amino acid sequence set forth in SEQ ID NO: 1.

22. The method according to Claim 19, wherein the variant thrombin comprises the amino acid sequence set forth in SEQ ID NO: 2.

23. The method according to Claim 19, wherein the variant thrombin further comprises the amino acid substitution E217A.

24. The method according to Claim 23, wherein the variant thrombin comprises the amino acid sequence as set forth in SEQ ID NO: 3.

25. The method according to Claim 23, wherein the variant thrombin is a variant thrombin B-chain comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 4.

26. The method according to Claim 19, wherein the variant thrombin has a PA/FC ratio greater than 1.0.

27. The method according to Claim 19, wherein the variant thrombin has a PA/FC ratio greater than 150.

28. The method according to Claim 19, wherein the physiologically acceptable composition further comprises a pharmaceutically acceptable carrier.

29. The method according to Claim 19, wherein the blood is in a blood vessel selected from the group consisting of an artery, an arteriole, a venule, a vein, a capillary, a fistula and a heart.

30. The method according to Claim 19, wherein the blood is in a cardiovascular device connected to the vascular system of an animal or human and selected from the group consisting of a stent, a vascular graft, an arterio-venous shunt, a cardiopulmonary bypass device, a cardiac assist device, a hemodialyzer and an artificial organ.

31. The method according to Claim 19, wherein the effective amount of the variant thrombin is delivered to the lumen of a blood vessel of a recipient animal or human.

32. The method according to Claim 19, wherein the effective amount of the variant thrombin is delivered to the blood as a bolus amount.

33. The method according to Claim 19, wherein the effective amount of the variant thrombin is delivered to the blood over a sustained period.

34. The method according to Claim 19, wherein the effective amount of the variant thrombin is delivered to blood of the animal or human by a route selected from the group consisting of an intravascular, an intraperitoneal, an intramuscular, an intrathecal, an intraarticular, an intrapulmonary, an intraperitoneal, a retroperitoneal, an intrapleural, a subcutaneous, a percutaneous, a transmucosal, an oral, a gastro-intestinal, and an intraocular route.

35. The method according to Claim 19, wherein the effective amount of the variant thrombin is delivered to the animal or human by an intravascular route.

36. The method according to Claim 19, wherein the effective amount of the variant thrombin is delivered to the animal or human by an intravascular infusion route selected from the group consisting of an intravascular injection, an intravascular drip and a catheter.

37. The composition according to Claim 19, wherein the effective amount of the variant thrombin is administered at the dosage of between about 0.1 μg/kg/day to about 30 mg/kg/day.

38. A method of inhibiting the formation of a thrombus, comprising the steps of:

(a) delivering to the blood of an animal or human a physiologically acceptable composition comprising an effective amount of a variant thrombin with substantially reduced procoagulant activity, wherein the variant thrombin has the amino acid substitutions W215A and comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 1; and

(b) allowing the variant thrombin to activate protein C, thereby inhibiting thrombus formation.

39. The method according to Claim 38, wherein the variant thrombin is a variant thrombin B-chain comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 2.

40. A method of inhibiting the formation of a thrombus, comprising the steps of:

(a) delivering to the blood of an animal or human a physiologically acceptable composition comprising an effective amount of a variant thrombin with substantially reduced procoagulant activity, wherein the variant thrombin has the amino acid substitutions W215A and E217A and comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 3; and

(b) allowing the variant thrombin to activate protein C, thereby inhibiting thrombus formation.

41. The method according to Claim 40, wherein the variant thrombin is a variant thrombin B-chain comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 4.

42. A kit comprising a variant thrombin comprising an amino acid sequence selected from SEQ ID NOS: 1 and 2, and packaging comprising instructions for using the variant prothrombin to induce antithrombotic activity in a recipient animal or human according to the method of Claim 19.

43. The kit according to Claim 42, further consisting a pharmaceutically acceptable carrier and instructions for use in delivering the variant prothrombin to an animal or human.

44. A kit comprising a variant thrombin with reduced procoagulant and platelet activating activity and comprising an amino acid sequence selected from SEQ ID NOS: 3 and 4, and packaging comprising instructions for

using the variant thrombin as an antithrombotic agent in a recipient animal or human according to the method of Claim 19.

45. The kit according to Claim 44, further comprising a pharmaceutically acceptable carrier and instructions for use in delivering the variant thrombin to an animal or human.

46. A method to determine the endogenous antithrombotic potential of the protein C system of an animal or patient, comprising the steps of:

(a) administering to an animal or human an effective dose of a variant thrombin having a substantially reduced fibrinogen cleavage activity and capable of activating protein C;

(b) obtaining from the animal or human a blood sample, and measuring the coagulation rate or APC amidolytic activity thereof; and

(c) comparing the coagulation rate or APC amidolytic activity to the coagulation rate or APC amidolytic activity of a standard, thereby indicating the endogenous antithrombotic potential of the protein C system of the animal or human.

47. The method according to Claim 46, wherein the variant thrombin comprises an amino acid sequence selected from SEQ ID NOS: 1 and 3.

48. The method according to Claim 53, further wherein the variant thrombin is a variant thrombin B-chain comprising an amino acid sequence at least 80% identical to the amino acid sequence selected from SEQ ID NO: 2 and SEQ ID NO: 4.

49. A kit comprising a variant thrombin with reduced procoagulant activity and comprising the amino acid sequence selected from SEQ ID NOS: 1, 2,

3 and 4, and packaging comprising instructions for using the variant thrombin to determine the endogenous antithrombotic potential of the protein C system of an animal or human according to Claim 49.

50. A method for producing activated protein C, comprising the steps of:

(a) obtaining an sample of protein C;

(b) incubating the sample of protein C with a variant thrombin with reduced procoagulant activity, wherein the variant thrombin has the amino acid substitution W215A and comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 1; and

(c) cleaving the isolated protein C by the variant thrombin, thereby yielding activated protein C.

51. The method according to Claim 50, further comprising the step of isolating the activated protein C substantially free of the variant thrombin and from fibrinogen cleavage activity.

52. The method according to Claim 50, wherein the variant thrombin is a variant thrombin B-chain comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 2.

53. The method according to Claim 57, wherein the variant thrombin further comprises the amino acid substitution E217A.

54. The method according to Claim 57, wherein the variant thrombin comprises an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 3.

55. The method according to Claim 57, wherein the variant thrombin is a variant thrombin B-chain comprising an amino acid sequence at least 80% identical to the amino acid sequence set forth in SEQ ID NO: 4:

56. A method of determining the protein C activity in an individual, comprising thesteps of:

(a) obtaining a blood sample from an individual;

(b) contacting the blood sample with a variant thrombin substantially free of fibrinogen cleavage activity and capable of protein C activation; and

(c) measuring the level of activated protein C in the blood sample.

57. The method of Claim 62, further comprising the step of adding to the variant thrombin a thrombomodulin analog, calcium ions, and an optional activated protein C chromogenic substrate.

58. The method of Claim 62, wherein the variant thrombin is selected from SEQ ID NOS: 1, 2, 3 and 4.